REMARKS

Claims 7-12 and 16-18 are now pending in the application. Claims 13-15 are cancelled herein. Claims 17 and 18 are new. Support for the present amendments can be found throughout the application as filed. The Examiner is respectfully requested to reconsider and withdraw the rejections in view of the amendments and remarks contained herein.

EXAMINER'S INTERVIEWS DATED APRIL 8 AND MAY 11, 2009

Applicants' representative acknowledge and appreciate the Examiner extending the courtesy to discuss the claims and pending rejections discussed during the two telephonic interviews dated April 8 and May 11, 2009. Applicants have amended the claims according to the suggestions made by the Examiner during the interviews. Applicants have responded to the Interview Summary mailed April 15, 2009 and have filed the response into the record on May 13, 2009.

REJECTION UNDER 35 U.S.C. § 112

Claims 7-16 stand rejected under 35 U.S.C. § 112, first paragraph, for reasons similar to those of record set forth with regard to the similar subject matter of claims 1-6, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope to that as is now claimed.

Applicants have amended Claim 7 to recite:

"An assay to screen anti-malarial drugs by testing for binding of a test compound with plasmodium 90 kDa heat shock protein which comprises:
(a) immobilizing said test compound covalently on a matrix thereby forming an immobilized test compound;
(b) reacting saponin-freed Plasmodial trophozoite lysate comprising plasmodium 90 kDa heat shock protein with said immobilized test compound;
(c) detecting binding of plasmodium 90 kDa heat shock protein to said immobilized test compound;
(d) selecting said test compound if binding between said plasmodium 90 kDa heat shock protein and said immobilized test compound is detected in step (c);
(e) measuring growth of *Plasmodium falciparum* in an assay comprising measuring the number of *P. falciparum* ring forms growing into *P. falciparum* trophozoite forms with and without said selected test compound, said number of ring forms and said trophozoite forms being measured with flow cytometry;
(f) comparing the growth of *P. falciparum* in said assay with and without said selected test compound; and
(g) detecting a decrease in said measured growth of *P. falciparum* exposed to said selected test compound as compared to the growth of *P. falciparum* not exposed to said selected test compound as being indicative of said selected test compound being an anti-malarial drug."

The Action's allegations of "unconnected determinations" have been corrected by the specific amendments of Claims 7 and 17. Essentially there are two processes embodied by Claims 7 and 17. First, a test compound is immobilized onto a matrix and the immobilized test compound is reacted with a plasmodial trophozoite lysate comprising plasmodium 90 kDa heat shock protein (PfHSP90). The test compound is selected, if the immobilized test compound is detected as binding with the 90 kDa heat shock protein.

The second process in Claim 7 and 17 describes using the selected test compound (free of the matrix to which it was bound in the earlier process) in an anti-

malarial assay to measure and detect the inhibitory capabilities of the selected test compound against the target organism *P. falciparum*.

These steps are specifically spelt out and disclosed in the specification as filed using geldanamycin as an example test compound. The first process of Claim 7 and 17 using geldanamycin to bind to PfHSP90 is discussed in Example 3.0, pages 7-10 of the specification as filed. The anti-malarial assays using geldanamycin and flow cytometry are specifically taught on page 10 of the specification.

Applicants have clarified in the present amendments to Claims 7 and 17 that a test compound is first immobilized to a matrix and subsequently tested to see whether the immobilized test compound is capable of binding to PfHSP90. Then a selecting step has been added to the claims to clearly distinguish that the test compound and not the immobilized version of the test compound is subsequently selected and used in the anti-malarial assays to determine whether the selected test compound is in fact an anti-malarial drug.

If the Office prefers to further distinguish the immobilized test compound from the selected test compound (i.e. the test compound not bound to the matrix) used in the anti-malarial assays, step (e) can be amended by way of examiner's amendment to recite:

(e) measuring growth of *Plasmodium falciparum* in an assay comprising measuring the number of *P. falciparum* ring forms growing into *P. falciparum* trophozoite forms with and without said selected test compound **being free of said matrix**, said number of ring forms and said trophozoite forms being measured with flow cytometry;

Applicants respectfully submit that the amendments to Claims 7 and 17 have addressed the Office Action's allegation that the "Applicant teaches unconnected determinations in which a matrix-immobilized test compound is tested for binding with the *Plasmodium falciparum* heat shock protein of approximately 90kDa (PfHSP90) and the test compound, free of the matrix and free of the PfHSP90 in parasite lysate, is tested for its ability to inhibit the growth of a *Plasmodium falciparum* culture."

Claims 7-16 are rejected under 35 U.S.C. § 112, first paragraph for reasons similar to those of record as containing subject matter, which allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope to that as is now claimed. This rejection is respectfully traversed.

The Office Action further states that the therapeutic potential based upon the mere detection of binding is entirely unknown because, other than inhibition of ATP binding, there would appear no art accepted mode of action that would allow one to predict from the in vitro binding assay portion of the method that binding to the PfHSP90 would have any effect on parasite growth in that portion of the method, or in vivo.

Applicants respectfully submit that the present enablement rejection presented above has been overcome by linking the binding portion as characterized by the Action with an anti-malarial assay portion encompassed by the amended steps of Claims 7 and 17. Therefore, the amended method now positively recites in an active and present tense fashion, not only binding and detection of test compounds to PfHSP90, but

further, selection of test compounds capable of binding to PfHSP90 and determination of biological anti-malarial activity of the test compound thereby selected, to provide demonstrated therapeutic potential in the Applicants' anti-malarial drug screening assay.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the present rejection of Claim 1 and claims dependent thereon under 35 U.S.C. § 112, first paragraph. New Claim 17 is believed to be patentable over the cited rejections of Claims 7-16 for at least the reasons provided above with respect to Claim 7.

Claims 7-16 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action states that Claim 7 and claims dependent thereon the term "the presence" lacks antecedent basis. The phrase "said protein bound test compound" is unclear and that "saponin-free" should be "saponin-freed".

Applicants have amended Claim 7 to remove, "the presence", "protein bound test compound" and "saponin-free" as recommended in the present Action.

Claim 11 and claims dependent thereon allegedly recite an improper Markush group to describe methods for detecting plasmodium 90 kDa heat shock protein to immobilized test compound. Applicants have amended Claim 11 to remove the Markush language and replaced with alternative language "or" as suggested in the Office Action.

Claim 13 is alleged to recite "the number" without proper antecedent basis. Applicants have cancelled Claim 13 rendering this rejection moot.

Claims 14-16 reciting method steps having the term "using" is alleged to be improper method steps. Applicants have removed all instances of the term "using" in the claims as amended.

Claims 15 and 16 are alleged to have interrelationships and method steps that are not clear.

Applicants have amended Claim 16 and cancelled Claim 15, replacing Claim 15 with Claim 17. New Claim 17 recites blocking the carboxylate groups on the matrix not involved with bonding to amine groups on the derivatized test compound with ethanolamine. The volume of tris buffer is equal to the volume of plasmodial trophozoites, and the bound PfHSP90 protein bound to the immobilized test compound can be detected using the methods of Claim 18. The rejection in regards to Claim 15 is moot in view of the cancellation of Claim 15. In Claim 16, "said test compound of unknown structure" is urged to lack antecedent basis. Applicants have deleted "unknown structure" in Claim 16 rendering this rejection moot.

Applicants submit that all of the alleged issues stated in the present rejection of Claims 7-12 and 16 under 35 U.S.C. § 112, second paragraph have been overcome by the present amendments. Applicants respectfully request the Examiner to reconsider and withdraw the present rejection of Claims 7-12 and 16 under 35 U.S.C. § 112, second paragraph.

REJECTION UNDER 35 U.S.C. § 103

Claims 7-13 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Jendoubi et al. (J. Immunol. 134: 1941, 1985, hereinafter referred to as "Jendoubi") in view of Bonnefoy et al. (Mol. Biochem. Parasitol. 67: 157, 1994, hereinafter referred to as "Bonnefoy") and Banumathy et al. (J. Biol. Chem. 277: 3902, 2002, hereinafter referred to as "Banumathy") for reasons similar to those of record in the prior rejection of similar subject matter of Claims 1-4 and 6. This rejection is respectfully traversed.

Jendoubi teaches the isolation of a monoclonal antibody that was determined to have bound to a polypeptide from *Plasmodium falciparum* having an apparent molecular weight of 90,000 Da. Identification of the 90,000 Da. polypeptide as being PfHsp90 is alleged to be supplied from Bonnefoy. Bonnefoy is drawn to the characterization of the *P. falciparum* Pfhsp90 polypeptide by nucleotide sequencing. The Action alleges that the use of saponin in the extraction of PfHsp90 from host hsp 90 was provided by the teachings of Banumathy. The Action generally asserts that the references clearly teach that an immobilized test compound which bound the *Plasmodium falciparum* heat shock protein of approximately 90 kDa (PfHSP90) was also tested for its ability to inhibit the growth of the parasite.

The Applicants respectfully submit, that the cited art of record fails to teach each and every claim limitation of the newly amended Claim 7 and claims dependent thereon and therefore, fails to raise a *prima facie* case of obviousness with respect to these newly amended claims. (See MPEP § 2143.03).

Applicants have amended Claim 7 to recite:

> (e) measuring growth of *Plasmodium falciparum* in an assay comprising measuring the number of *P. falciparum* ring forms growing into *P. falciparum* trophozoite forms with and without said selected test compound, said number of ring forms and said trophozoite forms being measured with flow cytometry" and
> (g) detecting a decrease in said measured growth of *P. falciparum* exposed to said selected test compound as compared to the growth of *P. falciparum* not exposed to said selected test compound as being indicative of said selected test compound being an anti-malarial drug.

Jendoubi singly or in combination fails to teach an anti-malarial drug screening assay employing the various steps recited in the above amended Claim 7. For example, none of the references alone or in combination teach or fairly suggest a method step for measuring the number of *P. falciparum* ring forms growing into *P. falciparum* trophozoite forms with flow cytometry. Moreover, neither Jendoubi nor Bonnefoy fairly teach or suggest "detecting a decrease in said measured growth *of P. falciparum*" step in any putative assay since the test compound alleged to have been isolated in Jendoubi was not active against the malarial parasite. Therefore, one of ordinary skill in the art would not have concluded that there is a motivation or suggestion to combine the teachings of Jendoubi with the teachings of Bonnefoy and Banumathy to arrive at the presently amended claims.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the present rejection of Claims 7-13 under 35 U.S.C. § 103(a).

CONCLUSION

It is believed that all of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests

that the Examiner reconsider and withdraw all presently outstanding rejections. It is believed that a full and complete response has been made to the outstanding Office Action and the present application is in condition for allowance. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (248) 641-1600.

Respectfully submitted,

Dated: May 20, 2009

By: _____
Robert M. Siminski, Reg. No. 36,007
Fernando Alberdi Ph.D., Reg. No. 62,688

HARNESS, DICKEY & PIERCE, P.L.C.
P.O. Box 828
Bloomfield Hills, Michigan 48303
(248) 641-1600

RMS/FEA/akb